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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/797,613	03/09/2004	Brian Zambrowicz	07705.0001-01000	3971

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/797,613	ZAMBROWICZ ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-35 and 38-45* is/are pending in the application.

4a) Of the above claim(s) *21-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34,35 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1-18-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment and declaration filed 1-18-07 has been entered. Claims 34, 35, 40, 41 and 45 have been amended. Claims 36, 37 and 46 have been canceled. Claims 21-35 and 38-45 are pending. Claims 34, 35 and 38-45 are under consideration.

Double Patenting

Claim 38 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 39. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). A transgenic mouse is a mouse whose cellular genome, including somatic cells and germ cells, comprises a transgene or a targeting vector. Therefore, both somatic cells and germ cells will comprise said transgene or targeting vector. It is unclear what would be difference between a somatic transgenic mouse and a germ line transgenic mouse.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 34, 35 and 38-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants' amendment filed 1-18-07 necessitates this new ground of rejection.

The phrase "introducing a collection of mouse embryonic stem (ES) cells" in amended claim 34 is considered new subject matter. Applicants point out support for the amended claim 34 is at page 6, lines 3-20 and page 31, lines 17-25. Pages 6 and 31 discuss making, organizing and indexing libraries of mutated animal cells or any eukaryotic cells having genes that have been simultaneous mutated by one or more of the describe mutagenic components. A "collection of mouse ES cells" can mean a plurality of different types of mouse ES cells or a plurality of same type mouse ES cells. The specification only discuss introducing the describe vector into any eukaryotic cells that can be genetically manipulated and grown in culture. The specification fails to provide sufficient support for the phrase "introducing a collection of mouse embryonic stem (ES) cells". Thus, the phrase set forth above is considered new matter. Claims 35 and 38-45 depend from claim 34.

The phrase "identifying at least one mouse ES cells comprising the vector" on line 15 of claim 34 and the phrase "making a transgenic mouse...from at least one identified mouse ES cell that comprises the vector" on lines 18-19 of claim 34 are considered new subject matter. Applicants point out support for the amended claim 34 is at page 6, lines 3-20 and page 31, lines 17-25. Page 6, lines 3-20, discusses identifying eukaryotic cells having mutated gene(s) using the described vector. The specification fails to provide sufficient support for "identifying at least one mouse ES cells comprising the vector" or "making a transgenic mouse...from at least one

identified mouse ES cell that comprises the vector". Thus, the phrases set forth above are considered new matter.

The phrase "an internal ribosome entry site operatively positioned between said promoter and an initiation codon of said exon sequence" in amended claim 40 is considered new subject matter. Applicants point out support for amended claim 40 is on page 4, lines 3-14. Page 4, lines 3-14, only discusses a 3' gene trap cassette comprising in operably combination, a promoter, an exon (characterized by a translation initiation codon and open reading frame **and/or internal ribosome entry site**). There is no description regarding the positional order of a translation initiation codon and the internal ribosome entry site. The amended claim 40 requires an internal ribosome entry site operatively positioned between a promoter and an initiation codon of said exon sequence, however, the specification fails to provide sufficient support for such amendment. Thus, the phrase set forth above is considered new matter.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 34, 35 and 38-45 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and is repeated for

the reasons set forth in the preceding Official action mailed 7-19-06. Applicant's arguments filed 1-18-07 have been fully considered but they are not persuasive.

Applicants argue that the specification disclose the use of different selectable markers, promoters, numerous criteria for selecting candidate natural exons, and different types of vectors for introduction into ES cells. Applicants argue that the claimed method is enabled without undue experimentation, and the mice produced the claimed method can be used to determine the effect of a particular genetic mutation on the efficacy of a drug (amendment, p. 18-21). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 7-19-06. The claims encompass making a somatic transgenic mouse or a germ line transgenic mouse comprising a vector comprising a 3' gene trap cassette by introducing said vector into murine embryonic stem (ES) cells and selecting a murine ES cell comprising said vector. The specification fails to provide adequate guidance and evidence for how to make a somatic transgenic mouse or a germ line transgenic mouse comprising the claimed 3' gene trap cassette by using murine ES cells. The specification also fails to provide adequate guidance and evidence for how to use the produced somatic transgenic mouse or a germ line transgenic mouse for the study of basic biological processes and the development of therapeutics and diagnostics for diseases. 3' gene trap vector is designed to integrate into introns or genes such that the gene integrated is over-expressed, silenced, or under-expressed, and a fusion protein encoded by the exon sequence in the vector and the exon sequence of the integrated gene is expressed. The claimed method involves integrating 3' gene trap vector into unknown gene in mouse genome to create numerous unknown mutated genes that results in different transgenic mice. Although it was known in the art to use various selectable markers, promoters, and vectors for making a

transgenic mouse, however, it was unpredictable at the time of the invention whether a somatic transgenic mouse or a germ line transgenic mouse could be made by using the claimed method and whether there is any phenotype of the transgenic mouse produced by the claimed method. The claimed method must have a use, for example, producing a transgenic mouse having a phenotype for screening a drug. The transgenic mouse produced by the claimed method must have a use. It is unclear whether a somatic transgenic mouse or a germ line transgenic mouse could be made by using the claimed method and whether there is a genetic mutation of gene(s) or any phenotype of the transgenic mouse produced by the claimed method. Absent a genetic mutation of a gene or a phenotype of the transgenic mouse, one skilled in the art would not know how to use the transgenic mouse produced by the claimed method, for example, to determine the effect of a particular genetic mutation on the efficacy of a drug. Thus, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Applicants cite references Hawkins, Link, and Jones and argue that these references describe studies examining genotypic effect on drug efficacy. Applicants argue that usefulness of transgenic mice to determine the effect of a particular genetic mutation on the efficacy of a drug does not depend on whether the integrated gene is over-expressed, suppressed, or under-expressed. Any of those effects on an integrated gene could impact the efficacy of a drug (amendment, p. 21-22). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 7-19-06 and the reasons set forth above. The cited references do not use a 3' gene trap cassette to make transgenic mice and they fail to provide evidence for what kind of transgenic mice can be produced by using the claimed method and how to use said

produced transgenic mice to determine the effect of a particular genetic mutation on the efficacy of a drug. It was unpredictable at the time of the invention whether a somatic transgenic mouse or a germ line transgenic mouse could be made by using the claimed method and whether there is a genetic mutation of gene(s) and what type of genetic mutation produced via the 3' gene trap cassette or whether there is any phenotype of the transgenic mouse produced by the claimed method. Absent such guidance, one skilled in the art at the time of the invention would not know how to use the transgenic mouse produced by the claimed method, foe example, use the transgenic mice to determine the effect of a particular genetic mutation on the efficacy of a drug.

Applicants argue that the present claims do not recite a particular phenotype. The claims recite a method of making a transgenic mouse comprising the vector from at least one identified mouse ES cell. Applicants further argue that the specification teaches how to make a transgenic mouse having a vector integrated into its genome and there is no need for one skilled in the art to predict a phenotype (amendment, p. 22). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 7-19-06 and the reasons set forth above. The claimed method must have a use, for example, producing a transgenic mouse having a phenotype for screening a drug. The transgenic mouse produced by the claimed method also must have a use. The claimed method involves integrating 3' gene trap vector into unknown gene in mouse genome to create numerous unknown mutated genes that results in different transgenic mice having unknown and identified phenotype. Although it was known in the art to use various selectable markers, promoters, and vectors for making a transgenic mouse, however, it was unpredictable at the time of the invention whether a somatic transgenic mouse or a germ line transgenic mouse could be made by using the claimed method and whether there is any

phenotype of the transgenic mouse produced by the claimed method. Absent a genetic mutation of a gene or a phenotype of the transgenic mouse, one skilled in the art would not know how to use the transgenic mouse produced by the claimed method. Thus, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Applicants argue that one skilled in the art could use transgenic mice produced by the claimed method without characterizing the phenotype at all, for example, to determine the effect of the genotype of the mouse on the efficacy of a particular drug (amendment, p. 22-23). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 7-19-06 and the reasons set forth above. The specification fails to provide adequate guidance for how to determine "efficacy" of a drug by using a transgenic mouse. It appears that certain "phenotype" of the transgenic mouse is required to determine "efficacy" of a particular drug. Absent a phenotype, it is unclear how to determine "efficacy" of a particular drug associated with a particular genotype of a transgenic mouse.

Applicants argue that the enablement of the present claims does not require one skilled in the art to know or be able to predict the phenotype of transgenic mice made by the claimed method, one needs only be able to make and use a mouse comprising the vector from at least one identified mouse ES cell (amendment, p. 23). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 7-19-06 and the reasons set forth above. Absent a phenotype, one skilled in the art at the time of the invention would not know how to use the transgenic mouse produced by the claimed method.

Conclusion

No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

SHIN-LIN CHEN
PRIMARY EXAMINER